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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,247	08/14/2006	Tatsuya Nakai	294136US0X PCT	6936

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EXAMINER	
CHUI, MEI PING	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
09/17/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/589,247	NAKAI ET AL.	
	Examiner	Art Unit	
	MEI-PING CHUI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7-14,17-22 and 24-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7-14,17-22 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

Receipt of Request for Reconsideration filed on 08/10/2009 is acknowledged.

Claims 1, 4, 7-14, 17-22, 24-27 are pending in the application. Claims 2-3, 5-6, 15-16, 23 have been cancelled.

Upon further consideration, the examiner has new grounds of rejection; therefore, the finality of the rejection of the last office action is withdrawn. Accordingly, **THIS ACTION IS NON-FINAL**.

Status of Claims

Accordingly, claims 1, 4, 7-14, 17-22, 24-27 are presented for examination on the merits for patentability.

Rejection(s) and/or objection(s) not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Response to Arguments

Applicants argue the prior art Katsuma et al. teach that ethanol is a necessary component of the composition, which the composition, even in the presence of ethanol, does not irritat the skin; however, the secondary prior art Osborne et al. teach the reason (ethanol causes dehydration and undesirable irritating effects on the skin) for avoiding the use of ethanol that

does not exist in Katsuma et al. Hence, the rationale for combining Katsuma et al. with Osborne et al. is improper because there is no motivation to combine the references, especially when the instant claims does not require ethanol to be presented.

Applicants' arguments filed on 08/10/2009, with respect to previous rejections for claims 1, 4, 7-14, 17-22, 24-27 under 35 U.S.C. 103(a), have been considered and they are persuasive. The previous rejections of record are hereby withdrawn. However, upon further consideration and search, the Examiner has new grounds of rejection.

New ground of Claim Rejections

Claims 1, 4, 7-14, 17-22, 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawayanagi et al. (U. S. Patent No. 5,296,235) and Hidaka et al. (U. S. Patent No. 5,225,199) combined, and in view of Dasseux, J. L. H. (U. S. Patent Application Publication No. 2005/0101565).

Applicants Claim

Applicants claim an external preparation, i.e. plaster or poultice, comprising: (**A**) atorvastatin, or pitavastatin, or a salt thereof, (0.001-20 % by mass of the external preparation) and (**B**) at least one monoterpene (0.01-15 % by mass relative to the total amount of the external preparation); wherein (i) the monoterpene can be menthol, terpineol or citronellal, or a combination thereof; (ii) the external preparation further comprises: liquid paraffin, the styrene-isoprene-styrene copolymer and those recited therein; (iii) the preparation does not contain ethanol.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Sawayanagi et al. teach a plaster preparation that is suitable for cutaneous application and can avoid the risks of side effects caused by the drug, such that the use of the drug in the form of a plaster can help to promote the clinical utility of the drug (column 1, background section).

Sawayanagi et al. teach that the plaster preparation, which contains the active drug, can comprise a combination of constituents, such as:

(i) water-soluble polymers, polyacrylic acid and/or sodium polyacrylate, preferably in 0.5-10 % by weight of the plaster preparation (column 2, lines 14-25);

(ii) an absorbefacient compound for promoting cutaneous absorption, i.e. propylene glycol, menthol and the like, in 0.1-15 % by weight of the plaster preparation (column 2, lines 26-33);

(iii) additives that are commonly added to conventional hydrophilic base-type plaster preparation: polyhydric alcohols, i.e. sorbitol, glycerol; inorganic fillers, i.e. kaolin (4 grams); surfactants, i.e. polyethylene glycol monolaurate; pH modifiers and the like (column 2, lines 34-45; column 3-4, Example 1);

(iv) hydrophobic polymers, i.e. styrene-isoprene-styrene block copolymer in 0.2-20 %, or 30-99.5 % by weight of the plaster preparation (column 2, lines 58-61, line 65 to column 3, line 3);

(v) additional additives that are commonly added to conventional hydrophobic base-type plaster preparation, i.e. aliphatic hydrocarbon resins; plasticizer, i.e. liquid paraffin; pH modifiers (column 3, lines 1-14);

(vi) other additional additives, i.e. 70 % aqueous solution of D-sorbitol (15 grams); water; glycerin (15 grams) (column 3-4, Example 1).

Sawayanagi et al. also teach that, for a plaster preparation, the composition typically comprises 0.5-20 % by weight of the drug (column 3, lines 31-34).

With respect to the component "tartaric acid", it is known that tartaric acid is a common pH adjusting agent.

With respect to the claim limitation where the external preparation does not contain ethanol, the teaching of Sawayanagi et al. meets the limitation because it does **not teach the use of ethanol in the preparation of plaster is necessary and none of the examples contain ethanol.

Hidaka et al. teach a preparation of a transdermal plaster, which is capable of enhancing the absorption for clinically effective drugs for human skin application, comprising inorganic fine particles, i.e. silicate salts or aluminosilicate compounds; a usual adhesive, i.e. polyisoprene rubber; a diffusion auxiliary, i.e. polyethylene glycol, sorbitol, fluid paraffin, water (column 3, lines 45-49; column 4, lines 17-19; column 6, lines 12-14; column 7, lines 15-18; column 14, lines 56-66).

Hidaka et al. also teach that the inorganic fine particles, i.e. silicate salts or aluminosilicate compounds, is desirably presented in an amount between 0.001-1 % by weight in order to avoid skin rash (column 6, lines 29-34).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

(1) Sawayanagi et al. and Hidaka et al. do not teach the drug uses in the plaster is pitavastatin, or atorvastatin, or a salt thereof, as claimed.

(2) Sawayanagi et al. and Hidaka et al. do not teach the preparation is a poultice or the preparation contains carmellose sodium and the amounts, as claimed.

(3) Sawayanagi et al. and Hidaka et al. also do not teach the monoterpene used in the plaster preparation is terpineol or citronellal, or a combination thereof, as claimed. However, the deficiencies are cured by Dasseux, J. L. H.

Dasseux, J. L. H. teaches statins, i.e. pitavastatin, atrovastatin, and the pharmaceutically acceptable salt thereof, are inhibitors of cholesterol synthesis block cholesterol synthesis by inhibiting HMGCoA, the key enzyme involved in the cholesterol biosynthetic pathway. However, side effects, including liver and kidney dysfunction which associated with the use of these drugs have been reported (page 4: [0024]; page 11: [0086]). Dasseux, J. L. H. thus teaches that a pharmaceutical composition that comprises pharmaceutical active agent, i.e. statins, for treating, preventing, or managing cholesterol, dyslipidemia disorders and methods of reducing or avoiding an adverse effect associated with such active agent therapy would be desirable (page 6: [0044], [0049]).

Dasseux, J. L. H. also teaches the composition can be used in the preparation of different suitable dosage forms, i.e. transdermal in the forms of a plaster or cataplasm (e.g. poultice), for administration to a patient (page 17: [0206]). Dasseux, J. L. H. further teaches that a suitable

amount of disintegrant (preferably in 1-5 % by weight), i.e. croscarmellose sodium, can be used in the preparing the dosage form, depending on the type of formulation (page 18: [0224]).

Finding of prima facie obviousness Rational and Motivation

(MPEP 2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Sawayanagi et al. and Hidaka et al. with Dasseux, J. L. H. to arrive at the instant invention.

One of ordinary skill would have been motivated to employ statins, i.e. pitavastatin or atrovastatin, in the preparation of a plaster for transdermal delivering these drugs to a patient because oral administration of these drugs would cause unwanted side effects, such as liver and kidney dysfunction; therefore an alternative delivery route that can help to avoid the risks of side effects caused by the drug and can promote the clinical utility of these drugs would be favorable and desired, as suggested by the prior art.

One of ordinary skill in the art also would have been motivated to incorporate common additives, i. e. polyethylene glycol or disintegrant, into a plaster preparation and then modify the amounts of these additives to a desirable level, depending on the type of selected formulation, as taught by Hidaka et al. and Dasseux, J. L. H.

With respect to the recitation of monoterpene is terpineol or citronellal as claimed, the prior art Sawayanagi et al. teach the plaster preparation uses menthol as an absorbefacient compound for promoting cutaneous absorption; such teaching would motivate one of ordinary skill in the art to try not only menthol, but also to try other monoterpenes, i.e. terpineol and

citronellal, because menthol, terpineol and citronellal are all functional equivalent monoterpenes; and thus, they can be used interchangeably.

From the teaching of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed external formulation. Therefore, the invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowed.

Contact Information

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Thursday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where the application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either PRIVATE PAIR or PUBLIC PAIR. Status information for unpublished applications is available through PRIVATE PAIR only. For more information about

the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the PRIVATE PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/H. C./

Examiner, Art Unit 1616

/Mina Haghighatian/
Primary Examiner, Art Unit 1616